HFA-305 Div. of Dockets Mgt.

MAR 4 2005

Approval Date:_____

FREEDOM OF INFORMATION SUMMARY

SUPPLEMENTAL NEW ANIMAL DRUG APPLICATION

NADA 038-233

RALGRO
(zeranol)

This supplement provides for deletion of the no residue designation and regulatory method and addition of a tolerance for zeranol of 20 ppb in edible tissues of sheep published in 21 CFR 556.760.

Sponsored by:

Schering-Plough Animal Health Corp.
1095 Morris Ave.
Union, NJ 07083

2005-38-233

FOIS 1

FREEDOM OF INFORMATION SUMMARY

RALGRO
Feedlot Lambs

1. GENERAL INFORMATION:

a. File Number:	NADA 038-233
b. Sponsor:	Schering-Plough Animal Health Corp. 1095 Morris Ave. Union, NJ 07083 Drug Labeler Code: 000061
c. Established Name:	Zeranol
d. Propriety Name:	RALGRO
e. Dosage Form:	Implantation (ear implant) as per 21 CFR 522.2680
f. How Supplied:	Each carton contains ten 24-dose cartridges (12 mg dose).
g. How Dispensed:	OTC
h. Amount of Active Ingredients:	12 mg zeranol.
i. Route of Administration:	Subcutaneous implantation on the posterior aspect of the middle one-third of the ear by means of an implant gun.
j. Species/Class:	Feedlot lambs.
k. Recommended Dosage:	One implant containing 12 mg zeranol.
l. Pharmacological Category:	Steroid hormone.
m. Indications:	For increased rate of weight gain and improved feed conversion of growing lambs.
n. Effect of Supplement:	This supplement provides for deletion of the no residue designation and regulatory method and addition of a tolerance for zeranol of 20 ppb in edible tissues of sheep published in 21 CFR 556.760.

2. DRUG EFFECTIVENESS:

No new effectiveness data are required for the approval of this supplement. The product's effectiveness in feedlot lambs has been established in the supplemental approval published in the Federal Register August 28, 1970 (pp. 13727-13728), for RALGRO (NADA 038233).

3. TARGET ANIMAL SAFETY:

No new target animal safety data are required for the approval of this supplement. The product's safety in feedlot lambs has been established in the supplemental approval published in the Federal Register August 28, 1970 (pp. 13727-13728), for RALGRO (NADA 038233).

4. HUMAN SAFETY:

The product's human food safety for feedlot lambs has been established in the supplemental approval published in the Federal Register August 28, 1970 (pp. 13727-13728), for RALGRO (NADA 038233).

A. Toxicology

Summaries of pivotal toxicology studies of zeranol can be found in earlier FOI Summaries for this NADA, particularly the FOI Summary dated January 1989 for the supplemental approval dated July 28, 1989, which describes the data supporting the deletion of the requirement for a withholding time for zeranol in cattle.

B. Residue Chemistry

The submission of residue data was not required for approval of this supplemental application. No changes have been made in the conditions of use, which were established relative to the regulatory method having a sensitivity of 20 ppb in the edible tissues of sheep. Although the description of the method is deleted from 21 CFR 556.760, that method is still available from FDA (Center for Veterinary Medicine, 7500 Standish Place, Rockville, MD 20855) and applicable to the new tolerance of 20 ppb for edible tissues of sheep.

5. AGENCY CONCLUSIONS:

The data submitted in support of this NADA satisfies the requirements of section 512 of the Federal Food, Drug, and Cosmetic Act and 21 CFR Part 514 of the implementing regulations providing for the deletion of 1) the no residue designation and regulatory method and 2) addition of a tolerance for zeranol of 20 ppb in edible tissues of sheep published in 21 CFR 556.760. As previously written, 21 CFR 556.760 evidenced an inconsistency between cattle and sheep. In particular, the 'no residue' designation originally applied to zeranol in both cattle and sheep. But in assessing a subsequent supplemental application proposing deletion of the 65-day withholding time for cattle treated with zeranol, FDA concluded that zeranol's

toxicological properties are solely associated with its estrogenic activity (see January 1989 FOI Summary for approval dated July 28, 1989). FDA calculated an ADI and safe concentrations, and after a showing that the peak total residue concentrations in edible tissues of cattle were below the respective safe concentrations, concluded that a zero pre-slaughter withdrawal period was appropriate and that there was no need for a tolerance or regulatory method. Because the toxicology of a compound is determined independent of the target food animal, the sponsor asked that FDA make the changes noted above.

The Agency has concluded that the toxicological decisions made for cattle (subsequent to the original approvals for cattle and sheep) also apply to sheep. Moreover, since the original conditions of use were established with reference to the method's sensitivity of 20 ppb, the setting of a 20 ppb tolerance is a logical alternative. Approval of this supplemental application will have no impact on humans consuming tissues from sheep treated with zeranol.

The Center for Veterinary Medicine has concluded that, for this product, adequate directions for use by the layperson have been provided and the product will have over-the-counter (OTC) status. Label directions are accompanied by pictorial diagrams and detailed instruction in plain language. The drug is not a controlled substance. The product's status remains OTC. The labeling is adequate for the intended use.

This approval does not qualify for marketing exclusivity under section 512(c)(2)(F)(iii) of the Federal Food, Drug, and Cosmetic Act.

Under the Center's supplemental approval policy (21 CFR 514.106(b)(2)), this is a Category II change. The approval of this change is not expected to have any adverse effect on the safety or effectiveness of this new animal drug. Accordingly, this approval did not require a reevaluation of the safety and effectiveness data in the parent application.

No patent information was submitted by the sponsor with this application.

6. ATTACHMENTS:

Facsimile Labeling is attached as indicated below:

RALGRO (feedlot lambs) 10 24-Dose Cartridge Carton Label (RALOGUN)
RALGRO (feedlot lambs) Package Insert (RALOGUN)

SCHERING-PLOUGH CORPORATION
PACKAGING ARTWORK PRE-PRESS INFO

DATE: 11/2/04
DESIGNER: AF
PRODUCT/COMPONENT: RALGRO INSERT (FRONT)
QUANTITY/STRENGTH: 12 mg
RIC NUMBER: 24492613
DIMENSIONS: 241.5 mm X 133.5 mm
AFFECTED RIC: 24492605
OUTPUT RESOLUTION 100%
LTS#: 40276
BARCODE TYPE (NDC): N/A
BARCODE SIZE/X DIMENSION
HUMAN READABLE REQUIRED: YES NO
FULL NUMBER *(SYS. CHARACTER + NDC)*:
3-

BAR CODE: Supplier responsible for supplying actual LIVE bar code represented by "FPO" with magnification factor based on process requirements in accordance with UCC standards. Minimum acceptance criteria is grade "C" based on ANSI X3.182 "Bar Code Print Quality Guideline."
INK DRAWDOWNS: (Light, Target & Dark Limits) Five sets must be provided to Schering-Plough incoming inspection for approval. Color Standards must be approved by Schering-Plough.
PROOFS: Must be provided to the Labeling Control Analyst for approval. Proofs must be approved by Schering-Plough prior to printing. The supplier is not allowed to make any changes without written approval by Schering-Plough.

NOTE: For GTIN - Package Level Indicator set at 0 (zero).

FOR CARTONS: INTERLEAVED 2 OF 5 [RIC NUMBER] BAR CODE NEEDED ON TUCK FLAPS OR GLUE ENDS, AS PER APPROVED ART.

PANTONE COLORS
BLACK
PMS 186
PMS 153

PACKAGING COMPONENT APPROVAL

SUBMISSION # 2

1EXAMINE BLACK & WHITE COPY AND ACCOMPANYING COLOR BREAK.

	APPROVED	NOT APPROVED	DATE
DESIGNER	☐	☐	
COPY EDITOR	☐	☐	
MEDICAL	☐	☐	
TRADEMARKS	☐	☐	
PACKAGING	☐	☐	
SPECIFICATIONS	☐	☐	
MARKETING	☐	☐	
REGULATORY	☐	☐	

ART DUE DATE: INV. LOCATION:

SQA:
APPROVAL VERIFIED: DATE:

RALGRO (zeranol) is an anabolic agent which increases rate of weight gain and improves feed conversion of feedlot lambs.

Do not use in veal calves. Effectiveness and animal safety in veal calves have not been established.

RALGRO implanted lambs may be marketed 40 days following the last implant.

RALGRO pellets are stable when stored under normal conditions.

RALGRO pellets each contain 12 mg of zeranol. Only one pellet is required for a proper dose.

TAKE TIME

READ THE LABEL DIRECTIONS

WARNING: DO NOT IMPLANT ANIMALS WITHIN 40 DAYS OF SLAUGHTER. DO NOT ATTEMPT TO SALVAGE IMPLANT SITE FOR HUMAN OR ANIMAL FOOD. IMPLANT PELLETS IN THE EAR ONLY. ANY OTHER LOCATION MAY RESULT IN VIOLATION OF LAW

A WITHDRAWAL PERIOD HAS NOT BEEN ESTABLISHED IN PRERUMINATING CALVES. DO NOT USE IN CALVES TO BE PROCESSED FOR VEAL.

CAUTION: Not for use in animals intended for breeding purposes. Under certain management conditions, especially creep-fed lambs implanted at an early age, there have been occasional reports of vaginal and/or rectal prolapse, after implanting.

HAZARDOUS – NOT FOR HUMAN USE.

DOSAGE: 12 mg zeranol

A single pull of the RALGUN® injection trigger delivers the proper 12 mg dose (one 12-mg pellet per chamber).

Manufactured by a non-sterilizing process.

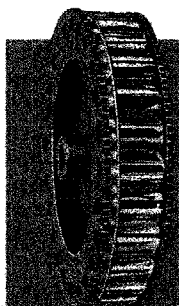
Store between 2° and 25°C (36° and 77°F).

Schering-Plough Animal Health
Schering-Plough Animal Health Corp
Union, NJ 07083

Made in Ireland.
24492613 Rev 9/04
This product may not be marketed or used in Ireland or elsewhere in the EU

RALGRO®

BRAND OF ZERANOL

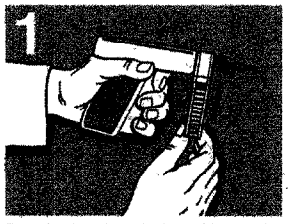


IMPLANTS IN CARTRIDGES FOR FEEDLOT LAMBS

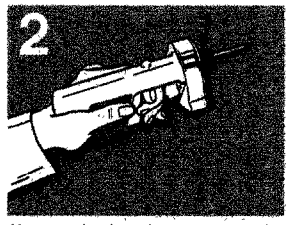
DIRECTIONS FOR USING

RALGRO®

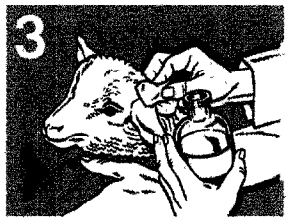
IN CARTRIDGES WITH THE RALOGUN® PELLET INJECTOR



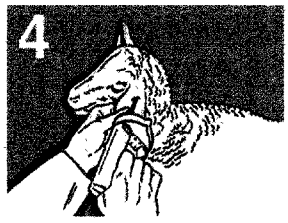
Each chamber of the plastic cartridge contains a full dose of RALGRO pellets. Insert the cartridge in the magazine of the RALOGUN injector with the hole in the axle of cartridge pointed toward the handle of the gun.



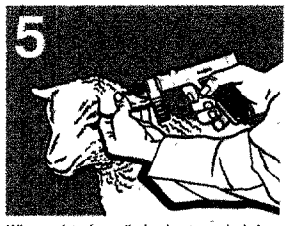
After snapping into place, rotate cartridge clockwise to ensure proper seating then check window at top to ensure pellet chamber is aligned with plunger.



Wipe outer surface of animal's ear with piece of cotton or gauze moistened with rubbing alcohol or suitable disinfectant.



Pierce the skin with the needle on the outside of the ear, at the middle part of ear. Direct the needle toward the base of the ear just under the skin, but not into the cartilage.



When point of needle is about one inch from site of puncture, depress trigger *once* to deposit one RALGRO implant, then carefully withdraw needle keeping trigger depressed and plunger extended.

Wipe needle with cotton swab saturated with alcohol or other suitable disinfectant before implanting the next lamb. Then rotate cartridge in direction of arrow until a new dose is visible and centered in window.

 NADA #38-233, Approved by FDA.

PANTONE COLORS	
BLACK	
PMS 186	
PMS 153	

SCHERING-PLOUGH CORPORATION
PACKAGING ARTWORK PRE-PRESS INFO

DATE: 11/2/04
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RIC NUMBER: 24492613
AFFECTED RIC: 24492605
LTS#: 40276

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DESIGNER: AF
QUANTITY/STRENGTH: 12 mg
DIMENSIONS: 241.5 mm X 133.5 mm
OUTPUT RESOLUTION 100%
BARCODE TYPE (NDC): N/A
BARCODE SIZE/X DIMENSION
HUMAN READABLE REQUIRED: YES ____ **NO** ____
FULL NUMBER *(SYS. CHARACTER + NDC)*:
3-
NOTE: For GTIN - Package Level Indicator set at 0 (zero).
FOR CARTONS: INTERLEAVED 2 OF 5 (RIC NUMBER) BAR CODE NEEDED ON TUCK FLAPS OR GLUE ENDS, AS PER APPROVED ART.

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REGULATORY	☐	☐	

ART DUE DATE: _____ INV. LOCATION: _____

SQA:
APPROVAL VERIFIED: _____ DATE. _____